

Attorney's Docket No. 026350-060Application No. 09/902,633

Page 5

REMARKS

Entry of the foregoing, reexamination, and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.112 are respectfully requested.

As correctly stated in the Office Action, Claims 16-19 are pending in the present application. Claims 16-19 stand rejected.

By the present amendment, Claims 16-19 have been amended to address the alleged informalities indicated on page 2 of the Office Action. Support for such amendment can be found throughout the originally-filed application. No new matter has been added. Moreover, none of the amendment to the claims were intended to limit the scope of any such claims or elements(s) recited therein.

Claim Objections

Claims 16-19 stand objected to for various informalities listed on page 2 of the Office Action. Without conceding to the merits of this objection, and solely in an effort to expedite prosecution, Claims 16-19 have been amended as suggested by the Examiner. Withdrawal of these objections is respectfully requested.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 16-19 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled. This rejection is respectfully traversed.

Applicants respectfully submit that the present application is enabled for the scope of the claims. The Office Action asserts that the specification is enabling for the detection of a specific hairpin structure. The Office Action also alleges that the

Attorney's Docket No. 026350-060Application No. 09/902,633

Page 6

specification does not provide guidance regarding how to distinguish between double stranded DNA, normal single stranded DNA, and a highly ordered structural site and that no parameters are provided to distinguish a highly-ordered structural site. However, it is unclear to Applicants why the method and probe must distinguish between DNA and RNA for the present invention to be enabled. The claims are directed to detecting a highly ordered structural site using a probe, not distinguishing between RNA and DNA. Additionally, the Office Action provides no technical reasoning as to why the presently claimed method and device is likely only capable of detecting the specific hairpin structure exemplified, rather than other highly-ordered structures.

Further, as discussed below, a definition for highly-ordered structural sites is provided on the first page of the specification. Thus, in light of the teachings in the specification as well as the contemporary knowledge in the field, Applicants respectfully submit that the skilled artisan could readily practice the invention.

Finally, to particularly rebut the Examiner's contention that the presently claimed invention is specific only to the hairpin structure discussed in the specification, Applicants provide additional technical data. The following examples relate to "highly ordered structural sites" other than hairpin DNA structure. Applicants express their willingness to provide the following Examples in the form of a declaration should the Examiner deem such action necessary.

Example 1

Applicants investigated the effect of the probe according to the presently claimed invention using thermal melting temperature (T_m) of the double stranded DNAs having the following structures, instead of the electrochemical response

discussed in the specification. Conventionally, a T_m value is used as an index of stability of a double stranded DNA. An increase in T_m indicates stabilization of the double stranded structure of DNA.

Using a buffer comprising 10 mM MES, 1 mM EDTA (pH 6.2), 0.1 M NaCl, and 10 μ M of the probe according to the presently claimed invention, stability (T_m) of the double stranded DNAs was measured at the DNA concentration of 0.9 mM. In this measurement, T_m was measured on a normal DNA (DNA 1), a mismatch DNA (DNA 2) and a bulge DNA (DNA 3). DNA 2 contains an A-A pair that does not interact and DNA 3 contains a single stranded portion of AAAA (bulge structure) that does not interact.

As shown in Table 1, the mismatch DNA and the bulge DNA exhibited T_m stabilization of +1.0 and +6.0, respectively. This means that the probe of the presently claimed invention binds to the mismatch or the single stranded portion of the DNAs described in Table 1, resulting in stabilization of the double stranded structure of the DNAs. The same result was obtained with an electrochemical measurement used in the presently claimed invention.

Table 1

DNA #	DNA structure	ΔT_m ($^{\circ}$ C)
1	AAAAAAAAAAAAAAAAAAAA TTTTTTTTTTTTTTTTTTTT	0
2	AAAAAAAAAAAAAAAAAAAA TTTTTTT A TTTT TTTTT A	+1.0
3	AAAAAAAAAAAAAAAAAAAA TTTTTTT T TTTTTTT AAAA	+6.0

Example 2

Using a buffer comprising 10 mM MES, 1 mM EDTA (pH 6.2), 0.1 M NaCl, and 3.3 μ M of the probe according to the presently claimed invention, stability (T_m) of the double stranded DNAs was measured at the DNA concentration of 0.9 mM. In this measurement, T_m was measured on a normal DNA (DNA 1), a mismatch DNA (DNA 2), and a bulge DNA (DNA 3). DNA 2 contains an A-G pair that does not interact and DNA 3 contains a single stranded AT-GT pair that does not interact.

As shown in Table 2, the mismatch DNA and the bulge DNA exhibited T_m stabilization of +11 and +13, respectively. This means that the probe of the presently claimed invention binds to the mismatch or the single stranded portion of the DNAs described in Table 2, resulting in stabilization of the double stranded structure of the DNA. Applicants note that the same result was obtained with an electrochemical measurement used in the presently claimed invention.

Table 2

DNA #	DNA	ΔT_m ($^{\circ}$C)
1	ATTGACCGTAATGGGATAGG TAACTGGCATTACCCTATCC	0
2	ATTGACCGTAATGGGATAGG TAACTGGCAT ACCCTATCC G	+11
3	ATTGACCGTAATGGGATAGG TAACTGGCAT CCCTATCC GT	+13

Attorney's Docket No. 026350-060Application No. 09/902,633

Page 9

Applicants respectfully submit that the above results clearly demonstrate that the presently claimed invention is enabled for more than just the specific hairpin structure as alleged by the Examiner on page 3 of the Office Action.

In view of the above, withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 16-19 stand rejected under 35 U.S.C. § 112, second paragraph, as purportedly being indefinite. In particular, the Office Action indicates that the specification does not provide a definition of a "highly-ordered structural site." This rejection is respectfully traversed.

Applicants respectfully submit that "highly ordered structure" is defined, at least, on page 1, second paragraph under section 2 of the instant specification:

A highly ordered structural site of a single stranded nucleic acid is a region located in a part of high-order structure of a DNA or RNA where the bases of the single stranded nucleic acids are not stacked, the region including a mismatch structure of an oncogenic DNA, a hairpin structure of a viral RNA, and a bulge.

Thus, contrary to the Examiner's assertion, a definition for "highly-ordered structural site" is given in the specification. From this description, one skilled in the art would clearly understand that a highly ordered structure is not merely a single stranded DNA but is an irregular region of a double stranded DNA.

In light of the above, withdrawal of the rejection under 35 U.S.C. § 112, second paragraph, is respectfully requested.

Attorney's Docket No. 026350-060
Application No. 09/902,633
Page 10

Conclusions

From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.


If there are any questions concerning this amendment, or the application in general, the Examiner is respectfully requested to telephone Applicant's undersigned representative so that prosecution may be expedited.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

Date: February 17, 2004

By:


Jennifer A. Topmiller, Ph.D.
Registration No. 50,435

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620